EXHIBIT A: AMENDMENTS TO U.S. PATENT APPLICATION SERIAL NO. 09/494,332 (ATTORNEY DOCKET NO. 2094/1E285-US1)

SUBMITTED PURSUANT TO 37 C.F.R. § 1.121(b)(1)(iii) and § 1.121(c)(1)(ii)

IN THE SPECIFICATION:

The paragraph at lines 18-26 on page 15 of the specification has been amended as follows:

The sample is then subjected to reverse transcription using (a) random primers, such as random hexamer primers obtained from Pharmacia Biotech, Piscataway, NJ, and/or (b) primers derived from the 5' or 3' non-coding regions of the HCV RNA genomic sequence. Reverse transcription is carried out using conventional procedures, such as are described in *Current Protocols in Molecular Biology*, Volumes I, II, and III, 1997 (F.M. Ausubel ed.); in U.S. Patent No. 5,322,770; in Young, et al., *J. Clin. Microbiol.* 31(4):882 (1993); Myers et al., *Biochemistry* 30(3):7661 (1991); or as described in [copending] provisional patent application Serial No. 60/118,520, filed February 3, 1999 [attorney docket number 2094/0E287].

IN THE CLAIMS:

Claims 1, 10, 16, 25 and 31 have been amended as follows:

1. (Amended) A method for [co-detecting] detecting Hepatitis C Virus (HCV) RNA [and] or Human Immunodeficiency Virus (HIV) RNA in a biological sample, said method comprising:

(A) performing a reverse transcription reaction using RNA derived from said sample as a template and at least one reverse transcription primer that will prime reverse transcription of DNA from HCV RNA and at least one reverse transcription primer that will prime reverse transcription of DNA from HIV RNA to produce reverse transcription products comprising (a) HCV-specific reverse transcription products, (b) HIV-specific reverse transcription products, or (c) a combination of (a) and (b);

(B) amplifying said reverse-transcription products using one or more pairs of oligonucleotide primers specific for the 5' noncoding region of HCV and one or more pairs of oligonucleotide primers specific for HIV to produce amplification products comprising (a) HCV-specific amplification products, (b) HIV-specific amplification products, or (c) a combination of (a) and (b);

wherein each of said pairs of oligonucleotide primers specific for HCV comprises:

(i) forward primer 5'-GGGAGAGCCATAGTGGTCTGCGGAA-3' (C131F25) <SEQ ID NO. 1>, and

(ii) reverse primer 5'-CGGGGCACTCGCAAGCACCCTATCA-3' (C294R25) <SEQ ID NO. 2>;

wherein each of the pairs of oligonucleotide primers specific for HIV-1 comprises a forward primer with the sequence:

5'-CTGCTTAAGCCTCAATAAAGCTTGCCTTGA-3' (JBLTR4) <SEQ ID NO. 3>, and a reverse primer specific for HIV-1 selected from the group consisting of:

(1) 5'-GGGTCTGAGGGATCTCTAGTTACC AGAGT-3' (JBLTR6) <SEQ ID NO. 4>, and

(2) 5'-TGTTCGGGCGCCACTGCTAGAGA-3' (JBLTR8) <SEQ ID NO. 5>,

wherein each of the pairs of oligonucleotide primers specific for HIV-2 comprises a forward primer with the sequence 5'-GGGAGGTTCTCTCCAGCACTAGCA-3' (2LTRe) <SEQ ID NO. 6>, and a reverse primer specific for HIV-2 with the sequence 5'-GCGACTAGGAGAGATGGGAACACACA-3' (2LTR-R1) <SEQ ID NO. 7>; and

(C) detecting said amplification products;

wherein detection of HCV-specific amplification products indicates the presence of HCV RNA in said sample, detection of HIV-specific amplification products indicates the presence of HIV RNA in said sample, and the detection of HCV-specific amplification products and HIV-specific amplification products indicates the presence of HCV RNA and HIV RNA in said sample.

10. (Amended) A method for [co-amplifying] amplifying Hepatitis C Virus (HCV) DNA [and] or Human Immunodeficiency Virus (HIV) DNA, said method comprising:

(A) performing a polymerase chain reaction on a DNA sample suspected to contain HCV DNA, HIV DNA, or a combination of HCV DNA and HIV DNA, using one or more pairs of oligonucleotide primers specific for the 5' noncoding region of HCV and one or more pairs of oligonucleotide primers specific for HIV to produce amplification products comprising (a) HCV-specific amplification products, (b) HIV-specific amplification products, or (c) a combination of (a) and (b);

wherein each of said pairs of oligonucleotide primers specific for HCV comprises:

(i) forward primer 5'-GGGAGAGCCATAGTGGTCTGCGGAA-3' (C131F25) <SEQ ID NO. 1>, and

(ii) reverse primer 5'-CGGGGCACTCGCAAGCACCCTATCA-3' (C294R25) <SEQ ID NO. 2>;

wherein each of the pairs of oligonucleotide primers specific for HIV-1 comprises a forward primer with the sequence:

5'-CTGCTTAAGCCTCAATAAAGCTTGCCTTGA-3' (JBLTR4) <SEQ ID NO. 3>, and a reverse primer specific for HIV-1 selected from the group consisting of:

(1) 5'-GGGTCTGAGGGATCTCTAGTTACC AGAGT-3' (JBLTR6) <SEQ ID NO. 4>, and

(2) 5'-TGTTCGGGCGCCACTGCTAGAGA-3' (JBLTR8) <SEQ ID NO. 5>; and

wherein each of the pairs of oligonucleotide primers specific for HIV-2 comprises a forward primer with the sequence 5'-GGGAGGTTCTCTCCAGCACTAGCA-3' (2LTRe) <SEQ ID NO. 6>, and a reverse primer specific for HIV-2 with the sequence 5'-GCGACTAGGAGAGATGGGAACACACA-3' (2LTR-R1) <SEQ ID NO. 7>.

16. (Amended) A method for [co-detecting] <u>detecting</u> Hepatitis C Virus (HCV) RNA [and] <u>or</u> Human Immunodeficiency Virus (HIV) RNA in a biological sample, said method comprising:

(A) performing a reverse transcription reaction using RNA derived from said sample and internal positive control (IPC) RNA as a template, at least one reverse transcription primer that will prime reverse transcription of DNA from IPC RNA, at least one reverse transcription primer that will prime reverse transcription of DNA from HCV RNA, and at least one reverse transcription primer that will prime reverse transcription of DNA from HIV RNA to produce reverse transcription products comprising (a) IPC-specific reverse transcription products and (b) HCV-specific reverse transcription

products, (c) HIV-specific reverse transcription products, or (d) any combination of any of the foregoing;

(B) amplifying said reverse-transcription products using one or more pairs of oligonucleotide primers specific for IPC, one or more pairs of oligonucleotide primers specific for the 5' noncoding region of HCV, and one or more pairs of oligonucleotide primers specific for HIV to produce amplification products comprising (a) IPC-specific amplification products, (b) IPC-specific amplification products and HCV-specific amplification products, (c) IPC-specific amplification products and HIV-specific amplification products, or (d) a combination of any of the foregoing;

wherein each of said pairs of oligonucleotide primers specific for IPC comprises:

(1) forward primer 5'-CGCCAGCGTGGACCATCAAGTAGTAA-3' (IPCF1) <SEQ ID NO. 8>, and

(2) reverse primer 5'-CACGATCCTGGAGCAGACACTGAAGA-3' (IPCR1) <SEQ ID NO. 9>;

wherein each of said pairs of oligonucleotide primers specific for HCV comprises:

(i) forward primer 5'-GGGAGAGCCATAGTGGTCTGCGGAA-3' (C131F25) <SEQ ID NO. 10>, and

(ii) reverse primer 5'-CGGGGCACTCGCAAGCACCCTATCA-3' (C294R25) <SEQ ID NO. 11>; and

wherein each of the pairs of oligonucleotide primers specific for HIV-1 comprises a forward primer with the sequence:

5'-CTGCTTAAGCCTCAATAAAGCTTGCCTTGA-3' (JBLTR4) <SEQ ID NO. 3>, and a reverse primer specific for HIV-1 selected from the group consisting of:

(1) 5'-GGGTCTGAGGGATCTCTAGTTACC AGAGT-3' (JBLTR6) <SEQ ID NO. 4>, and

(2) 5'-TGTTCGGGCGCCACTGCTAGAGA-3' (JBLTR8) <SEQ ID NO. 5>,

wherein each of the pairs of oligonucleotide primers specific for HIV-2 comprises a forward primer with the sequence 5'-GGGAGGTTCTCTCCAGCACTAGCA-3' (2LTRe) <SEQ ID NO. 6>, and a reverse primer specific for HIV-2 with the sequence 5'-GCGACTAGGAGAGATGGGAACACACA-3' (2LTR-R1) <SEQ ID NO. 7>; and

(C) detecting said amplification products

wherein detection of IPC-specific amplification products indicates the presence of IPC RNA in said sample, detection of HCV-specific amplification products indicates the presence of HCV RNA in said sample, detection of HIV-specific amplification products indicates the presence of HIV RNA in said sample, and the detection of HCV-specific amplification products and HIV-specific amplification products indicates the presence of HCV RNA and HIV RNA in said sample.

25. (Amended) A method for [co-amplifying] amplifying Internal Positive Control (IPC) DNA, Hepatitis C Virus (HCV) DNA, [and] or Human Immunodeficiency Virus (HCV) DNA, said method comprising:

(A) performing a polymerase chain reaction on a DNA sample containing IPC DNA and suspected to contain HCV DNA, HIV DNA, or any combination of any of the foregoing, using one or more pairs of oligonucleotide primers specific for IPC, one or more pairs of oligonucleotide primers specific for the 5' noncoding region of HCV, and one or more pairs of oligonucleotide primers specific for HIV to produce amplification products comprising (a) IPC amplification products, (b) IPC amplification products and HCV-specific amplification products, (c) IPC amplification products and HIV-specific amplification products, or (d) a combination of any of (a), (b), and (c);

wherein each of said pairs of oligonucleotide primers specific for IPC comprises:

(i) forward primer 5'-CGCCAGCGTGGACCATCAAGTAGTAA-3' (IPCF1) <SEQ ID NO. 8>, and

(ii) reverse primer 5'-CACGATCCTGGAGCAGACACTGAAGA-3' (IPCR1) <SEQ ID NO. 9>;

wherein each of said pairs of oligonucleotide primers specific for HCV comprises:

(i) forward primer 5'-GGGAGAGCCATAGTGGTCTGCGGAA-3' (C131F25) <SEQ ID NO. 10>, and

(ii) reverse primer 5'-CGGGGCACTCGCAAGCACCCTATCA-3' (C294R25) <SEQ ID NO. 11>; and

wherein each of the pairs of oligonucleotide primers specific for HIV-1 comprises a forward primer with the sequence:

5'-CTGCTTAAGCCTCAATAAAGCTTGCCTTGA-3' (JBLTR4) <SEQ ID NO. 3>, and a reverse primer specific for HIV-1 selected from the group consisting of:

(1) 5'-GGGTCTGAGGGATCTCTAGTTACC AGAGT-3' (JBLTR6) <SEQ ID NO. 4>, and

(2) 5'-TGTTCGGGCGCCACTGCTAGAGA-3' (JBLTR8) <SEQ ID NO. 5>,

wherein each of the pairs of oligonucleotide primers specific for HIV-2 comprises a forward primer with the sequence 5'-GGGAGGTTCTCTCCAGCACTAGCA-3' (2LTRe) <SEQ ID NO. 6>, and a reverse primer specific for HIV-2 with the sequence 5'-GCGACTAGGAGAGATGGGAACACACA-3' (2LTR-R1) <SEQ ID NO. 7>.

31. (Amended) A kit <u>suitable</u> for co-detecting HCV RNA and HIV RNA in a biological sample, said kit comprising:

(a) a pair of oligonucleotide primers specific for the 5' noncoding region of HCV comprising:

(i) forward primer 5'-GGGAGAGCCATAGTGGTCTGCGGAA-3'

(C131F25) <SEQ ID NO. 10>, and

(ii) reverse primer 5'-CGGGGCACTCGCAAGCACCCTATCA-3'

(C294R25) <SEQ ID NO. 11>; and

(b) oligonucleotide primers specific for HIV-1 which comprise a forward primer with the sequence:

5'-CTGCTTAAGCCTCAATAAAGCTTGCCTTGA-3' (JBLTR4)

<SEQ ID NO. 3>, and a reverse primer specific for HIV-1 selected from the group consisting of:

(1) 5'-GGGTCTGAGGGATCTCTAGTTACC AGAGT-3'

(JBLTR6) <SEQ ID NO. 4>, and

(2) 5'-TGTTCGGGCGCCACTGCTAGAGA-3' (JBLTR8) <SEQ ID NO. 5>,and a pair of oligonucleotide primers specific for HIV-2 which comprise a forward primer with the sequence 5'-GGGAGGTTCTCTCCAGCACTAGCA-3' (2LTRe) <SEQ ID NO. 6>, and a reverse primer specific for HIV-2 with the sequence:

5'-GCGACTAGGAGAGATGGGAACACACA-3' (2LTR-R1)

<SEQ ID NO. 7>.